

amended hereinabove. New claims 27-28 have been added hereinabove. Accordingly, after entry of the instant amendment, Claims 23-28 will be pending and under consideration. A marked-up version of the claims to show the changes made by this amendment is attached hereto as **Exhibit A**. A clean version of all pending claims as amended herein is attached hereto as **Exhibit B**.

I. AMENDMENTS

Claims 25-26 have been amended to correct typographical errors. New Claim 27 recites, *inter alia*, pores in the glass surface of a magnetic particle having a diameter of less than 1 nm. Support can be found in the specification at page 6, lines 5-6. Claim 28 recites, *inter alia*, eluting bound nucleic acids from the magnetic particle. Support can be found in the specification at page 11, lines 6-9. No new matter has been added by these amendments.

II. OBJECTIONS

Claims 19-22 stand objected to because these claims are dependent on a nonelected claim. Applicants have canceled Claims 19-22, thus making this objection moot. Accordingly, Applicants respectfully request withdrawal of the objection.

The disclosure stands objected to because the specification does not contain headings designating different sections. In response, Applicant has amended the specification to correct these informalities herein and respectfully requests withdrawal of the objection.

III. REJECTIONS UNDER 35 U.S.C. § 103

Claims 19-26 stand rejected under 35 U.S.C. § 103 as being unpatentable over Groves *et al.*, European 0 343 934 (“Groves”) in view of Palladino, U.S. Patent No. 5,458,813 (“Palladino”) and Falleroni *et al.*, U.S. Patent No. 4,824,712 (“Falleroni”) and Woodard *et al.*, U.S. Patent No. 5,503,816 (“Woodard”) or Padhye *et al.*, U.S. Patent 5,658,548 (“Padhye”).

The Examiner states that Groves discloses magnetic particles having a core of magnetic material completely coated with a metal oxide coating, which can be SiO₂. These particles are prepared by mixing a solution of the magnetic material with a sol to form gel particles, and heating the gel particles to 250°C to 2000°C. The Examiner states that Palladino discloses introducing boron into porous gels by the sol-gel technique and further to form glass containing boron oxide. The Examiner states that Falleroni discloses coating a scored glass surface with a silica-boron sol-gel composition to form a glass coating. The Examiner states that Woodard discloses the use of glass powder to purify DNA and the binding and elution of DNA with boron silicate. The Examiner states that Padhye discloses the use of glass particles to separate DNA from other substances and mixtures of silica gel and glass particles to separate DNA. Assuming the use of SiO₂ with the magnetic particle of Groves, the Examiner concludes that it would be completely encapsulated in a essentially non-porous glass layer and further, that it would have been obvious to provide boron oxide in the glass layer as disclosed by Palladino and Falleroni to form a glass coating. The Examiner further concludes that since Groves discloses that magnetic particles can bind certain biological molecules other than nucleic acids, it would have been obvious to use magnetic particles to purify nucleic acids as suggested by

Woodard or Padhye, which disclose the use of glass particles to purify DNA. This rejection is respectfully traversed for the reasons set forth below.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. M.P.E.P. § 2143.

Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art. "The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art." *In re Kotzab*, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). See also *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

The test for obviousness is what the combined teachings of the references would have suggested to one of ordinary skill in the art, and all teachings in the prior art must be considered to the extent that they are in analogous arts. Where the teachings of two or more prior art references conflict, the examiner must weigh the power of each reference to suggest solutions to one of ordinary skill in the art, considering the degree to which one reference might accurately discredit another. *In re Young*, 927 F.2d 588, 18 USPQ2d 1089 (Fed. Cir. 1991)

The prior art must provide one of ordinary skill in the art with a reasonable expectation of success. The skilled artisan, in light of the teachings of the prior art, must have a reasonable expectation that the modification or combination suggested would succeed. *In re Dow*, 5 USPQ2d 1529, 1531-32 (Fed. Cir. 1988). The teaching or suggestion to make the claimed invention, as well as the reasonable expectation of success, must come from the prior art, not Applicants' disclosure. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). "Obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness." *In re Rinehart*, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976). *See also Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1207-08, 18 USPQ2d 1016, 1022-23 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991); *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988). *See* MPEP § 2143.02.

Groves teaches magnetic particles comprising certain types of magnetic materials encapsulated in a metal oxide, which can be SiO₂. Such particles can be used as supports for immobilised enzymes, antibodies, antigens and other bioactive materials (see Groves, col. 7, lines 56-58).

Nowhere does Groves teach or suggest a magnetic particle with an outer glass layer comprising boron oxide, as is required by the claims as presently amended.

Nor does Groves teach or suggest that the magnetic particles disclosed therein are even capable of binding to nucleic acids, as is also required by the claims as presently amended. Consequently, Groves also fails to teach any method of separating nucleic acids from a fluid containing the nucleic acids, much less the claimed method of doing so comprising the steps of contacting a fluid containing nucleic acids with magnetic

glass particles comprising boron oxide, allowing the nucleic acids to bind to the particles, and separating the bound nucleic acids from the fluid.

Palladino teaches introducing boron into porous gels for use in glass manufacture. Palladino does not remedy the deficiencies of Grove in that Palladino does not teach or suggest the separation of nucleic acids from a fluid.

Falleroni teaches coating a scored glass surface with a silica-boron sol-gel to form a glass coating. Falleroni does not remedy the deficiencies of Grove and Palladino in that Falleroni does not teach or suggest the separation of nucleic acids from a fluid.

Woodard teaches that silicon-containing materials, including boron silicate, can bind DNA from a suspension containing DNA and permit elution of the DNA from the silicon-containing materials material. Padhye teaches that mixtures of silica gel and glass particles, including borosilicate glass particles, in a suspension with chaotropic salts can be used to separate DNA from other substances. Neither Woodard nor Padhye remedy the deficiencies of Groves, Palladino and Falleroni in that neither Woodard nor Padhye teach or suggest that magnetic particles comprising boron oxide can be used to separate DNA from fluids. All pending claims require the separation of nucleic acids from a fluid by binding the nucleic acids to a magnetic glass particle comprising a boron oxide. No reference cited by the Examiner teaches the use of any magnetic glass particle for the separation of nucleic acids from a fluid.

Claim 28 adds the further step of eluting the nucleic acids from the magnetic glass particle comprising boron oxide. No reference cited by the Examiner teaches the elution of a nucleic acid from any magnetic glass particle.

Accordingly, the collection of references cited by the Examiner fails to render the claimed invention obvious, as they fail to teach each limitation of the currently

pending claims. Specifically, no reference discloses separation of nucleic acids from a fluid utilizing any magnetic particle. In addition, no reference discloses a method of eluting a nucleic acid from any magnetic particle, as is required by claim 28.

In addition, this combination of references is inadequate to render the present invention obvious because there is no suggestion or motivation to modify the references. Such a teaching, suggestion or motivation is not found explicitly or implicitly in the references or the knowledge general to one of ordinary skill in the art. At best, Palladino and Falleroni suggest that it is desirable to include boron oxide into the silicon dioxide surface of a magnetic particle for improved chemical properties. There is still no teaching that such a composition would be useful for the binding of nucleic acids, much less a method of doing so. In addition, nowhere in these references is there a suggestion that such a composition could even be useful for the elution of nucleic acids from its surface, much less a method of doing so. Groves, which is the only reference to discuss binding of bioactive materials to a magnetic glass bead, never discusses the elution of any bioactive material, and never discusses binding or elution of nucleic acids. Furthermore, there is no suggestion or motivation to combine these references with either Woodward or Padhye. Woodward only discusses the use of boron silicates, not borosilicate glass. In fact, Woodward suggests that glass beads are not suitable for DNA binding and recovery (see Woodward, col. 1, lines 55-56). In fact, there is no teaching or suggestion that borosilicate glass particles alone would be effective at all. Thus, this combination of references is insufficient to suggest the present invention.

Moreover, this combination is inadequate to render the present invention obvious because the cited references do not provide the skilled artisan with a reasonable expectation of success of achieving the invention of the amended claims. Taking a

magnetic particle with a metal oxide surface of silicon dioxide, converting such a surface to a borosilicate glass, and using such a composition to separate nucleic acid does not have the requisite degree of predictability. First, there is no teaching that the silicon dioxide surface of the particles disclosed in Groves are capable of binding nucleic acids. Second, it is unpredictable what effect converting a silicon dioxide surface of a magnetic particle to a borosilicate glass will have on its ability, if any, to bind to a nucleic acid. None of the cited references or the knowledge of one of ordinary skill in the art provides any predictability. Third, it is unpredictable what effect the magnetic properties of the particle will have on binding nucleic acids. Groves does not discuss the binding of nucleic acids on the magnetic particles disclosed therein. None of the other references even discusses magnetism. Indeed, prior to the present invention, it would be a surprising result if nucleic acids immobilized on magnetic particles would not be destroyed (see the specification at page 6, lines 18-20). Unexpectedly, the present inventors discovered that magnetic glass particles comprising a boron oxide could be used to separate nucleic acids from a fluid. (See specification, pages 18-22, example 3). Thus, there is no reasonable expectation of success provided by the cited references. Instead, these references merely offer an invitation for future experimentation. While the cited references may provide some incentive to try to separate nucleic acids using magnetic particles surrounded by a borosilicate glass layer, obvious to try is not the applicable standard. *See, In re O'Farrell*, 853 F.2d 894 (Fed. Cir. 1988).

For the reasons set forth above, Applicant respectfully requests reconsideration and withdrawal of this rejection.

IV. DOUBLE PATENTING REJECTION

Claims 19-26 stand rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-11 of U.S. Patent No. 6,255,477 B1. The Examiner asserted that Claims 19-26 would have been obvious from the magnetic particles and method of their use claimed by the patent.

In response, while not admitting that the claims of the above-identified patent application are not patentably distinct from claim 1-11 of U.S. Patent No. 6,255,477, Applicants, upon indication of allowable subject matter, will submit a Terminal Disclaimer under 37 C.F.R. § 1.321(c) of the above-identified application.

CONCLUSION

Entry of the foregoing amendments and remarks into the file history of the subject application is respectfully requested. Applicant believes this application is in condition for allowance, which is respectfully solicited. If any issue remains in connection herewith, the Examiner is respectfully invited to contact the undersigned to discuss same.

The Commissioner is authorized to charge all required fees, fees under 37 CFR § 1.17 and all required extension of time fees, or credit any overpayment, to Pennie & Edmonds, LLP U.S. Deposit Account No. 16-1150.

Respectfully submitted,

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EXHIBIT A

Application No. 09/756,743 filed January 10, 2001

Amendment of January 30, 2003

MARKED-UP VERSION OF THE CLAIMS TO SHOW CHANGES MADE

25. (Amended) The method of claim 23 wherein the bound nucleic acids are separated [form] from the fluid with a magnetic field.
26. (Amended) The method of claim 23 wherein the magnetic particle is not subjected to the influence of a magnetic [filed] field before being brought in contact with sample and is thus able to sediment when being brought in contact with the sample.